

10/587,613A Yong Chu 01/20/2010

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PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	AUG 10	Time limit for inactive STN sessions doubles to 40 minutes
NEWS	3	AUG 18	COMPENDEX indexing changed for the Corporate Source (CS) field
NEWS	4	AUG 24	ENCOMPLIT/ENCOMPLIT2 reloaded and enhanced
NEWS	5	AUG 24	CA/CAPLUS enhanced with legal status information for U.S. patents
NEWS	6	SEP 09	50 Millionth Unique Chemical Substance Recorded in CAS REGISTRY
NEWS	7	SEP 11	WPIDS, WPINDEX, and WPIX now include Japanese FTERM thesaurus
NEWS	8	OCT 21	Derwent World Patents Index Coverage of Indian and Taiwanese Content Expanded
NEWS	9	OCT 21	Derwent World Patents Index enhanced with human translated claims for Chinese Applications and Utility Models
NEWS	10	NOV 23	Addition of SCAN format to selected STN databases
NEWS	11	NOV 23	Annual Reload of IFI Databases
NEWS	12	DEC 01	FRFULL Content and Search Enhancements
NEWS	13	DEC 01	DGENE, USGENE, and PCTGEN: new percent identity feature for sorting BLAST answer sets
NEWS	14	DEC 02	Derwent World Patent Index: Japanese FI-TERM thesaurus added
NEWS	15	DEC 02	PCTGEN enhanced with patent family and legal status display data from INPADOCDB
NEWS	16	DEC 02	USGENE: Enhanced coverage of bibliographic and sequence information
NEWS	17	DEC 21	New Indicator Identifies Multiple Basic Patent Records Containing Equivalent Chemical Indexing in CA/CAPLUS
NEWS	18	JAN 12	Match STN Content and Features to Your Information Needs, Quickly and Conveniently
NEWS	19	JAN 25	Annual Reload of MEDLINE database
NEWS EXPRESS MAY 26 09 CURRENT WINDOWS VERSION IS V8.4, AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2009.			
NEWS HOURS	STN Operating Hours Plus Help Desk Availability		
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Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 18:29:28 ON 01 FEB 2010

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.22	0.22

FILE 'REGISTRY' ENTERED AT 18:29:44 ON 01 FEB 2010

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STRUCTURE FILE UPDATES: 31 JAN 2010 HIGHEST RN 1204295-01-1

DICTIONARY FILE UPDATES: 31 JAN 2010 HIGHEST RN 1204295-01-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 26, 2009.

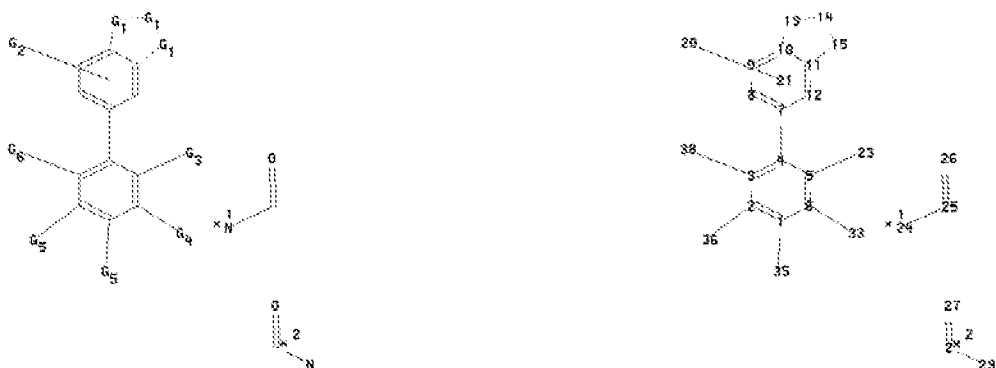
Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stdoc/properties.html>

=>

Uploading C:\Documents and Settings\ychu\Desktop\Case\10587613\10587613-02012010.str



```

chain nodes :
20 23 24 25 26 27 28 29 33 35 36 38
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
chain bonds :
1-35 2-36 3-38 4-7 5-23 6-33 24-25 25-26 27-28 28-29
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 10-13 11-12 11-15 13-
14
14-15
exact/norm bonds :
1-35 2-36 3-38 4-7 5-23 6-33 10-13 11-15 13-14 14-15 24-25 25-26 27-28
28-29
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12
isolated ring systems :
containing 1 :

```

G1:C,O,S,N

G2:O,CH,t-Bu,X,H

G3:H,CH3,Et,n-Pr

G4:[*1],[*2]

G5:H,CH3,Et,n-Pr,i-Pr,n-Bu,i-Bu,s-Bu,t-Bu,X

G6:H,CH3,Et,n-Pr,i-Pr,n-Bu,i-Bu,s-Bu,t-Bu,X

Match level :

```

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 20:CLASS 21:Atom 23:CLASS 24:CLASS
25:CLASS 26:CLASS
27:CLASS 28:CLASS 29:CLASS 33:CLASS 35:CLASS 36:CLASS 38:CLASS

```

=> d
L1 HAS NO ANSWERS
L1 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 18:31:53 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 12233 TO ITERATE

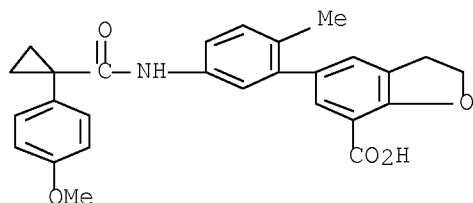
16.3% PROCESSED 2000 ITERATIONS 10 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 238031 TO 251289
PROJECTED ANSWERS: 754 TO 1692

L2 10 SEA SSS SAM L1

=> d scan

L2 10 ANSWERS REGISTRY COPYRIGHT 2010 ACS on STN
IN 7-Benzofurancarboxylic acid, 2,3-dihydro-5-[5-[[[1-(4-methoxyphenyl)cyclopropyl]carbonyl]amino]-2-methylphenyl]-
MF C27 H25 N O5



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

=> s l1 full
FULL SEARCH INITIATED 18:32:23 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 246035 TO ITERATE

100.0% PROCESSED 246035 ITERATIONS 958 ANSWERS
SEARCH TIME: 00.00.08

L3 958 SEA SSS FUL L1

```
=> save l3 temp
ENTER NAME OR (END):yc10587613/a
ANSWER SET L3 HAS BEEN SAVED AS 'YC10587613/A'
```

=>

Uploading C:\Documents and Settings\ychu\Desktop\Case\10587613\10587613A-02012010.str



```
chain nodes :
20 23 24 25 26 27 28 29 33 35 36 38 39
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
chain bonds :
1-35 2-36 3-38 4-7 5-23 6-33 13-39 24-25 25-26 27-28 28-29
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 10-13 11-12 11-15 13-14
14-15
exact/norm bonds :
1-35 2-36 3-38 4-7 5-23 6-33 10-13 11-15 13-14 13-39 14-15 24-25 25-26
27-28 28-29
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12
isolated ring systems :
containing 1 :
```

G1:C,O,S,N

G2:O,CH,t-Bu,X,H

G3:H,CH3,Et,n-Pr

G4:[*1],[*2]

G5:H,CH3,Et,n-Pr,i-Pr,n-Bu,i-Bu,s-Bu,t-Bu,X

G6:H,CH3,Et,n-Pr,i-Pr,n-Bu,i-Bu,s-Bu,t-Bu,X

Match level :

```
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 20:CLASS 21:Atom 23:CLASS 24:CLASS
```

25:CLASS 26:CLASS
 27:CLASS 28:CLASS 29:CLASS 33:CLASS 35:CLASS 36:CLASS 38:CLASS 39:Atom
 Generic attributes :
 39:
 Number of Carbon Atoms : less than 7
 Type of Ring System : Monocyclic

 Element Count :
 Node 39: Limited
 O,O2
 S,S2
 N,N2

L4 STRUCTURE UPLOADED

=> d

L4 HAS NO ANSWERS

L4 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s l4

SAMPLE SEARCH INITIATED 18:43:31 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 12233 TO ITERATE

16.3% PROCESSED 2000 ITERATIONS 0 ANSWERS
 INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
 SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
 BATCH **COMPLETE**
 PROJECTED ITERATIONS: 238031 TO 251289
 PROJECTED ANSWERS: 0 TO 0

L5 0 SEA SSS SAM L4

=> s l4 sam sss sub=l3

SAMPLE SUBSET SEARCH INITIATED 18:43:47 FILE 'REGISTRY'

SAMPLE SUBSET SCREEN SEARCH COMPLETED - 54 TO ITERATE

100.0% PROCESSED 54 ITERATIONS 0 ANSWERS
 SEARCH TIME: 00.00.01

PROJECTIONS (WITHIN SPECIFIED SUBSET): ONLINE **COMPLETE**
 PROJECTED ITERATIONS (WITHIN SPECIFIED SUBSET): 640 TO 1520
 PROJECTED ANSWERS (WITHIN SPECIFIED SUBSET): 0 TO 0

L6 0 SEA SUB=L3 SSS SAM L4

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION

FULL ESTIMATED COST

202.81

203.03

FILE 'CAPLUS' ENTERED AT 18:44:11 ON 01 FEB 2010
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FILE COVERS 1907 - 1 Feb 2010 VOL 152 ISS 6
FILE LAST UPDATED: 31 Jan 2010 (20100131/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Oct 2009

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=> s l3
L7 121 L3

=> file reg	SINCE FILE	TOTAL
COST IN U.S. DOLLARS	ENTRY	SESSION
FULL ESTIMATED COST	0.50	203.53

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STRUCTURE FILE UPDATES: 31 JAN 2010 HIGHEST RN 1204295-01-1
DICTIONARY FILE UPDATES: 31 JAN 2010 HIGHEST RN 1204295-01-1

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=> s l4 full sss sub=l3

FULL SUBSET SEARCH INITIATED 18:45:02 FILE 'REGISTRY'

FULL SUBSET SCREEN SEARCH COMPLETED - 958 TO ITERATE

100.0% PROCESSED 958 ITERATIONS

59 ANSWERS

SEARCH TIME: 00.00.01

L8 59 SEA SUB=L3 SSS FUL L4

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

45.99

249.52

FILE 'CAPLUS' ENTERED AT 18:45:08 ON 01 FEB 2010

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FILE COVERS 1907 - 1 Feb 2010 VOL 152 ISS 6

FILE LAST UPDATED: 31 Jan 2010 (20100131/ED)

REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2009

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Caplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2009.

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=> s l8

L9 9 L8

=> d ii as hitstr tot

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'AS' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'

The following are valid formats:

ABS ----- GI and AB
 ALL ----- BIB, AB, IND, RE
 APPS ----- AI, PRAI
 BIB ----- AN, plus Bibliographic Data and PI table (default)
 CAN ----- List of CA abstract numbers without answer numbers
 CBIB ----- AN, plus Compressed Bibliographic Data
 CLASS ----- IPC, NCL, ECLA, FTERM
 DALL ----- ALL, delimited (end of each field identified)
 DMAX ----- MAX, delimited for post-processing
 FAM ----- AN, PI and PRAI in table, plus Patent Family data
 FBIB ----- AN, BIB, plus Patent FAM
 IND ----- Indexing data
 IPC ----- International Patent Classifications
 MAX ----- ALL, plus Patent FAM, RE
 PATS ----- PI, SO
 SAM ----- CC, SX, TI, ST, IT
 SCAN ----- CC, SX, TI, ST, IT (random display, no answer numbers;
 SCAN must be entered on the same line as the DISPLAY,
 e.g., D SCAN or DISPLAY SCAN)
 STD ----- BIB, CLASS

 IABS ----- ABS, indented with text labels
 IALL ----- ALL, indented with text labels
 IBIB ----- BIB, indented with text labels
 IMAX ----- MAX, indented with text labels
 ISTD ----- STD, indented with text labels

 OBIB ----- AN, plus Bibliographic Data (original)
 OIBIB ----- OBIB, indented with text labels

 SBIB ----- BIB, no citations
 SIBIB ----- IBIB, no citations

 HIT ----- Fields containing hit terms
 HITIND ----- IC, ICA, ICI, NCL, CC and index field (ST and IT)
 containing hit terms
 HITRN ----- HIT RN and its text modification
 HITSTR ----- HIT RN, its text modification, its CA index name, and
 its structure diagram
 HITSEQ ----- HIT RN, its text modification, its CA index name, its
 structure diagram, plus NTE and SEQ fields
 FHITSTR ----- First HIT RN, its text modification, its CA index name, and
 its structure diagram
 FHITSEQ ----- First HIT RN, its text modification, its CA index name, its
 structure diagram, plus NTE and SEQ fields
 KWIC ----- Hit term plus 20 words on either side
 OCC ----- Number of occurrence of hit term and field in which it occurs

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All of the formats (except for SAM, SCAN, HIT, HITIND, HITRN, HITSTR, FHITSTR, HITSEQ, FHITSEQ, KWIC, and OCC) may be used with DISPLAY ACC to view a specified Accession Number.
 ENTER DISPLAY FORMAT (BIB):end

=> d 19 ibib abs hitstr tot

L9 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:360171 CAPLUS Full-text

DOCUMENT NUMBER: 150:374537

TITLE: Preparation of triazole fused heteroaryl compounds as p38 kinase inhibitors

INVENTOR(S): Pettus, Liping H.; Sham, Kelvin K. C.; Tasker, Andrew; Xu, Shimin

PATENT ASSIGNEE(S): Amgen Inc., USA

SOURCE: PCT Int. Appl., 88pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

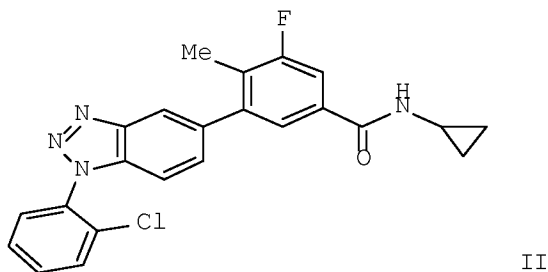
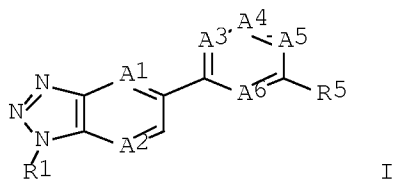
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009038784	A1	20090326	WO 2008-US10931	20080919
W:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: US 2007-994806P P 20070921

OTHER SOURCE(S): MARPAT 150:374537

GI



AB The title compds. I [A1 = CR2, N; A2 = CR3, N; A3 = CR4; A4-A6 = CR6, N (provided that no more than two of A3-A6 = N); R1 = alkyl, alkoxy, thioalkyl, etc.; R2, R3 = H, halo, haloalkyl, etc.; R4 = H, halo, haloalkyl, etc.; R5 = CONR7R8, CONR7R8, NR7COR7, etc.; R6 = H, halo, haloalkyl, etc.; R7 = H, alkyl, alkenyl, etc.; R8 = partially or fully satd. or unsatd. 3-8 membered monocyclic, 6-12 membered bicyclic, 7-14 membered tricyclic ring system, etc.], useful for modulating the activity of p38 MAP kinase, were prepd. E.g., a multi-step synthesis of II, starting from 1-bromo-4-fluoro-3-nitrobenzene and 2-chloroaniline, was given. Exemplified compds. I were tested in various biol. tests (data given for representative compds. I). The invention further provides pharmaceutical compns. including one or more compds. I, use of such compds. and compns. for treatment of p38 MAP kinase mediated diseases including rheumatoid arthritis, psoriasis and other inflammatory disorders, as well as intermediates and processes useful for the prepn. of compds. I.

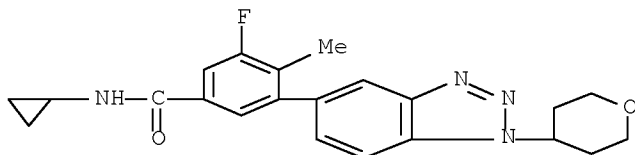
IT 1135352-10-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of triazole fused heteroaryl compds. for lowering plasma concns. of TNF- α , IL-1, IL-6, IL-8 or a combination thereof)

RN 1135352-10-1 CAPLUS

CN Benzamide, N-cyclopropyl-3-fluoro-4-methyl-5-[1-(tetrahydro-2H-pyran-4-yl)-1H-benzotriazol-5-yl]- (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2008:1481200 CAPLUS Full-text

DOCUMENT NUMBER: 150:29003

TITLE: NF- κ B inhibitor-p38 MAP kinase inhibitor combination for the treatment of cancer and inflammatory diseases

INVENTOR(S): Fu, Haian; Liotta, Dennis C.; Thomas, Shala L.; Snyder, James P.

PATENT ASSIGNEE(S): Emory University, USA

SOURCE: PCT Int. Appl., 122pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008150899	A1	20081211	WO 2008-US65132	20080529
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES,				

FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE,
 KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD,
 ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH,
 PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM,
 TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU,
 IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK,
 TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,
 TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,
 AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2007-932125P P 20070529

OTHER SOURCE(S): MARPAT 150:29003

AB The invention is directed to combinations of compds. useful in the treatment and prevention of cancer and inflammatory conditions or diseases. In particular embodiments, the combinations comprise one or more compds. that are NF- κ B inhibitors or p38 MAPK inhibitors. The invention further provides pharmaceutical compns. and methods of treatment using the combinations. In one embodiment, the NF-KB inhibitor is a curcumin analog.

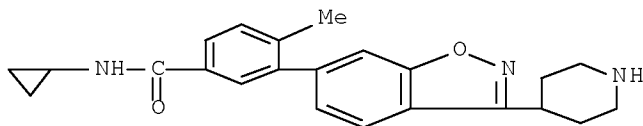
IT 651780-51-7 1092358-66-1

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(NF- κ B inhibitor-p38 MAP kinase inhibitor combination for treatment of cancer and inflammatory diseases)

RN 651780-51-7 CAPLUS

CN Benzamide, N-cyclopropyl-4-methyl-3-[3-(4-piperidinyl)-1,2-benzisoxazol-6-yl]- (CA INDEX NAME)



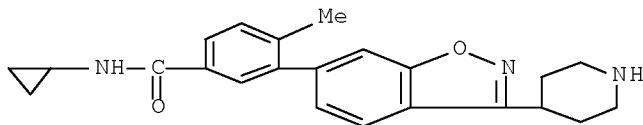
RN 1092358-66-1 CAPLUS

CN Benzamide, N-cyclopropyl-4-methyl-3-[3-(4-piperidinyl)-1,2-benzisoxazol-6-yl]-, mixt. with 3,5-bis[(2-fluorophenyl)methylene]-4-piperidinone (CA INDEX NAME)

CM 1

CRN 651780-51-7

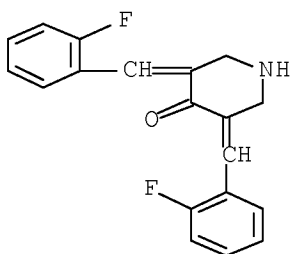
CMF C23 H25 N3 O2



CM 2

CRN 342808-40-6

CMF C19 H15 F2 N O



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
(2 CITINGS)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2008:1138529 CAPLUS Full-text

DOCUMENT NUMBER: 149:548255

TITLE: Kinase array design, back to front: Biaryl amides

AUTHOR(S): Baldwin, Ian; Bamborough, Paul; Haslam, Claudine G.;
Hunjan, Suchete S.; Longstaff, Tim; Mooney,
Christopher J.; Patel, Shila; Quinn, Jo; Somers, Don
O.

CORPORATE SOURCE: Medicines Research Centre, GlaxoSmithKline R&D,
Stevenage, Hertfordshire, SG1 2NY, UK

SOURCE: Bioorganic & Medicinal Chemistry Letters (2008),
18(19), 5285-5289
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 149:548255

AB New kinase inhibitors can be found by synthesis of targeted arrays of compds.
designed using system-based knowledge as well as through screening focused or
diverse compds. Most array strategies aim to add functionality to a fragment
that binds in the purine subpocket of the ATP-site. Here, an alternative
pharmacophore-guided array approach is described which set out to discover
novel purine subpocket-binding groups. Results are shown for p38.alpha. and
cFMS kinase, for which multiple distinct series with nanomolar potency were
discovered. Some of the compds. showed potency in cell-based assays and good
pharmacokinetic properties.

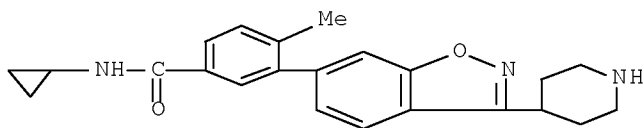
IT 651780-51-7 651780-52-8 651780-53-9

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
PRP (Properties); BIOL (Biological study)

(generation of biaryl amide kinase inhibitor lead compds. by addn. of
functionality to compds. already binding in the lipophilic interiors of
kinase ATP-binding sites to find structural fragments binding in the
purine subpockets)

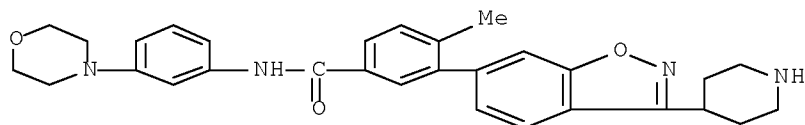
RN 651780-51-7 CAPLUS

CN Benzamide, N-cyclopropyl-4-methyl-3-[3-(4-piperidinyl)-1,2-benzisoxazol-6-
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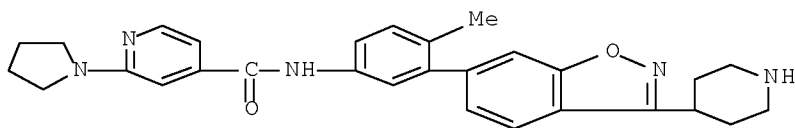
RN 651780-52-8 CAPLUS

CN Benzamide, 4-methyl-N-[3-(4-morpholinyl)phenyl]-3-[3-(4-piperidinyl)-1,2-benzisoxazol-6-yl]- (CA INDEX NAME)



RN 651780-53-9 CAPLUS

CN 4-Pyridinecarboxamide, N-[4-methyl-3-[3-(4-piperidinyl)-1,2-benzisoxazol-6-yl]phenyl]-2-(1-pyrrolidinyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2005:732643 CAPLUS Full-text

DOCUMENT NUMBER: 143:193999

TITLE: Preparation of fused heteroaryl derivatives as p38 kinase inhibitors

INVENTOR(S): Campos, Sebastien Andre; Swanson, Stephen; Walker, Ann Louise

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA

SOURCE: PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

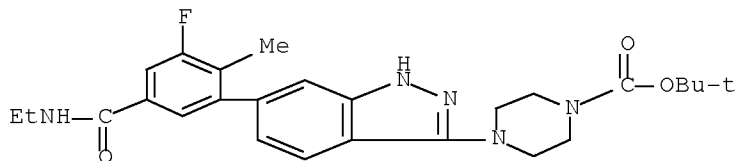
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005073219	A1	20050811	WO 2005-GB281	20050127
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,				

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
 LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
 NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
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 EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
 RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
 MR, NE, SN, TD, TG
 EP 1745038 A1 20070124 EP 2005-702034 20050127
 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR, LV
 JP 2007519695 T 20070719 JP 2006-550298 20050127
 US 20070142372 A1 20070621 US 2006-587614 20060728
 PRIORITY APPLN. INFO.: GB 2004-2140 A 20040130
 WO 2005-GB281 W 20050127
 ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
 OTHER SOURCE(S): CASREACT 143:193999; MARPAT 143:193999
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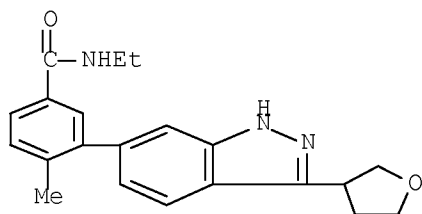
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [A = (un)substituted fused 5-membered heteroaryl ring, R1 = Me or Cl; R2 = NHCOR3 or CONH(CH2)qR4; R3 = H, alkyl, CF3, etc.; R4 = H, cycloalkyl, alkyl, etc.; q = 0-2; X and Y independently = H, Me or halo] and their pharmaceutically acceptable salts, are prepd. and disclosed as p38 kinase inhibitors. Thus, e.g., II was prepd. by coupling of N-cyclopropyl-3-fluoro-5-(1H-indazol-5-yl)-4-methylbenzamide (prepn. given) with 2-(bromomethyl)tetrahydro-2H-pyran. The activity of I was evaluated in fluorescence anisotropy kinase binding assays and it was revealed that compds. of the invention displayed IC50 values of <10 .mu.M or pKi values of >6. I as p38 kinase inhibitor should prove useful in the treatment of disease states mediated by p38 kinase. Pharmaceutical compns. comprising I are disclosed.
 IT 861972-51-2P 861972-52-3P 861972-53-4P
 861972-54-5P 861972-55-6P 861972-56-7P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of fused heteroaryl derivs. as p38 kinase inhibitors)
 RN 861972-51-2 CAPLUS
 CN 1-Piperazinecarboxylic acid, 4-[6-[5-[(ethylamino)carbonyl]-3-fluoro-2-methylphenyl]-1H-indazol-3-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



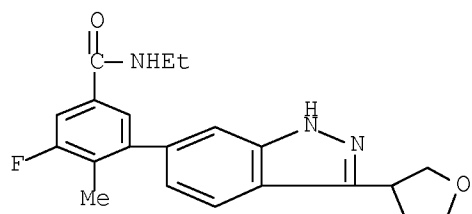
RN 861972-52-3 CAPLUS
 CN Benzamide, N-ethyl-4-methyl-3-[3-(tetrahydro-3-furanyl)-1H-indazol-6-yl]-

(CA INDEX NAME)



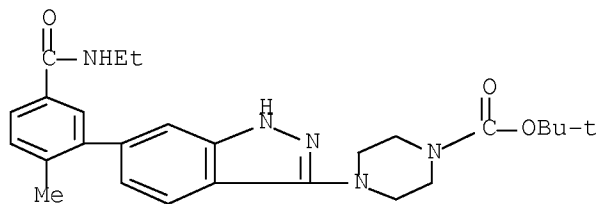
RN 861972-53-4 CAPLUS

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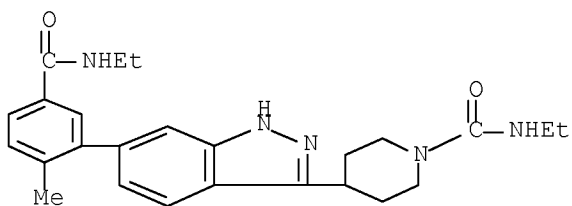
RN 861972-54-5 CAPLUS

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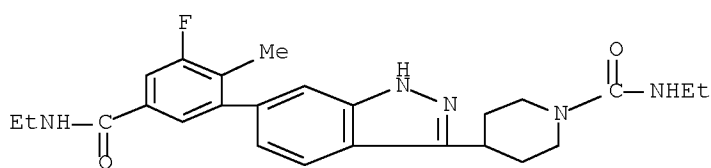
RN 861972-55-6 CAPLUS

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RN 861972-56-7 CAPLUS

CN 1-Piperidinecarboxamide, N-ethyl-4-[6-[5-[(ethylamino)carbonyl]-3-fluoro-2-methylphenyl]-1H-indazol-3-yl]- (CA INDEX NAME)



IT 861972-61-4P 861972-62-5P 861972-63-6P

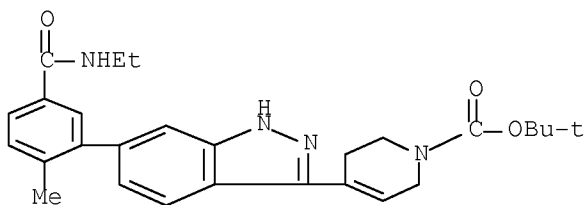
861972-65-8P 861972-66-9P 861972-67-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of fused heteroaryl derivs. as p38 kinase inhibitors)

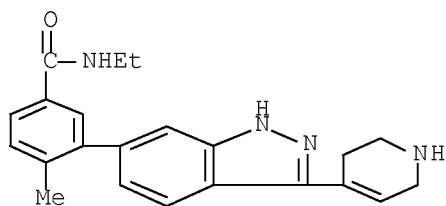
RN 861972-61-4 CAPLUS

CN 1(2H)-Pyridinecarboxylic acid, 4-[6-[5-[(ethylamino)carbonyl]-2-methylphenyl]-1H-indazol-3-yl]-3,6-dihydro-, 1,1-dimethylethyl ester (CA INDEX NAME)



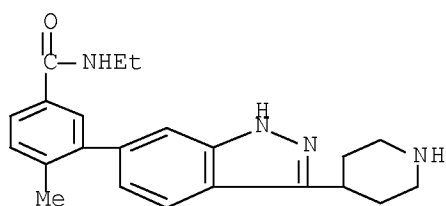
RN 861972-62-5 CAPLUS

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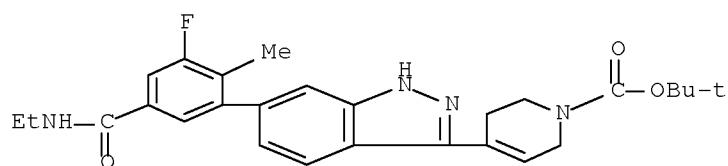
RN 861972-63-6 CAPLUS

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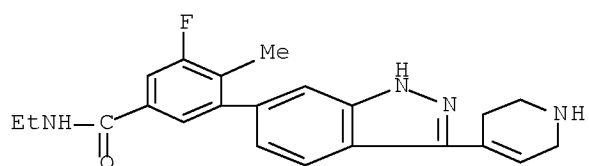
RN 861972-65-8 CAPLUS

CN 1(2H)-Pyridinecarboxylic acid, 4-[6-[5-[(ethylamino)carbonyl]-3-fluoro-2-methylphenyl]-1H-indazol-3-yl]-3,6-dihydro-, 1,1-dimethylethyl ester (CA INDEX NAME)

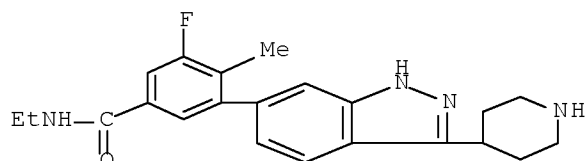


RN 861972-66-9 CAPLUS

CN Benzamide, N-ethyl-3-fluoro-4-methyl-5-[3-(1,2,3,6-tetrahydro-4-pyridinyl)-1H-indazol-6-yl]- (CA INDEX NAME)



RN 861972-67-0 CAPLUS
 CN Benzamide, N-ethyl-3-fluoro-4-methyl-5-[3-(4-piperidinyl)-1H-indazol-6-yl]-
 (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
 (1 CITINGS)
 REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2010 ACS on STN
 ACCESSION NUMBER: 2005:732641 CAPLUS Full-text
 DOCUMENT NUMBER: 143:211908
 TITLE: Preparation of fused heteroaryl derivatives as p38
 kinase inhibitors
 INVENTOR(S): Patel, Vipulkumar Kantibhai; Swanson, Stephen
 PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
 SOURCE: PCT Int. Appl., 54 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005073217	A1	20050811	WO 2005-GB266	20050127
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1709028	A1	20061011	EP 2005-702023	20050127
EP 1709028	B1	20081105		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR, IS				
JP 2007519693	T	20070719	JP 2006-550295	20050127
AT 413392	T	20081115	AT 2005-702023	20050127
ES 2314612	T3	20090316	ES 2005-702023	20050127
US 20070054942	A1	20070308	US 2006-587613	20060728
PRIORITY APPLN. INFO.:			GB 2004-2138	A 20040130
			WO 2005-GB266	W 20050127

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 143:211908; MARPAT 143:211908
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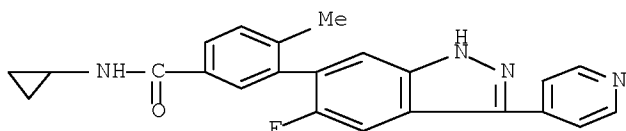
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [A = (un)substituted fused 5-membered heteroaryl ring, R1 = Me or Cl; R2 = NHCOR3 or CONH(CH2)qR4; R3 = H, alkyl, CF3, etc.; R4 = H, cycloalkyl, alkyl, etc.; q = 0-2; X and Y independently = H, Me or halo] and their pharmaceutically acceptable salts, are prepd. and disclosed as p38 kinase inhibitors. Thus, e.g., II was prepd. by palladium catalyzed coupling of 6-bromo-5-fluoro-3-(4-pyridinyl)-1H-indazole (prepn. given) with N-cyclopropyl-4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide. The activity of I was evaluated in fluorescence anisotropy kinase binding assays and it was revealed that compds. of the invention displayed IC50 values of <10 .mu.M or pKi values of >6. I as p38 kinase inhibitor should prove useful in the treatment of disease states mediated by p38 kinase. Pharmaceutical compns. comprising I are disclosed.

IT 862098-61-1P 862098-63-3P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of fused heteroaryl derivs. as p38 kinase inhibitors)

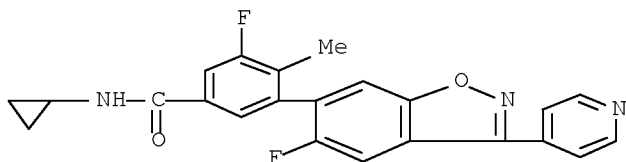
RN 862098-61-1 CAPLUS

CN Benzamide, N-cyclopropyl-3-[5-fluoro-3-(4-pyridinyl)-1H-indazol-6-yl]-4-methyl- (CA INDEX NAME)



RN 862098-63-3 CAPLUS

CN Benzamide, N-cyclopropyl-3-fluoro-5-[5-fluoro-3-(4-pyridinyl)-1,2-benzisoxazol-6-yl]-4-methyl- (CA INDEX NAME)



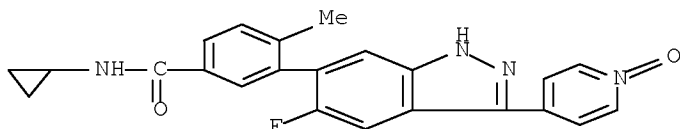
IT 862098-62-2P 862098-64-4P 862098-65-5P
862098-66-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of fused heteroaryl derivs. as p38 kinase inhibitors)

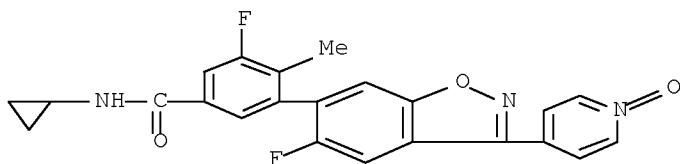
RN 862098-62-2 CAPLUS

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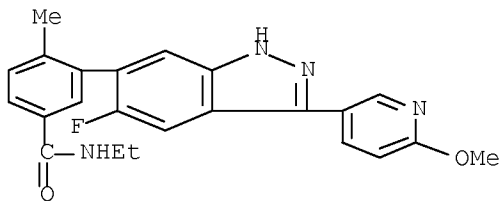
RN 862098-64-4 CAPLUS

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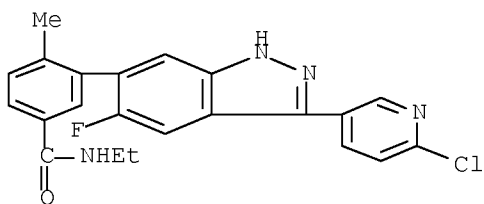
RN 862098-65-5 CAPLUS

CN Benzamide, N-ethyl-3-[5-fluoro-3-(6-methoxy-3-pyridinyl)-1H-indazol-6-yl]-4-methyl- (CA INDEX NAME)



RN 862098-66-6 CAPLUS

CN Benzamide, 3-[3-(6-chloro-3-pyridinyl)-5-fluoro-1H-indazol-6-yl]-N-ethyl-4-methyl- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2010 ACS on STN
 ACCESSION NUMBER: 2005:729633 CAPLUS Full-text
 DOCUMENT NUMBER: 143:211906
 TITLE: Preparation of fused heteroaryl derivatives as p38 kinase inhibitors
 INVENTOR(S): Bamborough, Paul; Campos, Sebastien Andre; Patel, Vipulkumar Kantibhai; Swanson, Stephen; Walker, Ann Louise
 PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
 SOURCE: PCT Int. Appl., 123 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005073189	A1	20050811	WO 2005-GB265	20050127
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1708996	A1	20061011	EP 2005-702022	20050127
EP 1708996	B1	20080827		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR, IS				
JP 2007519692	T	20070719	JP 2006-550294	20050127
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ES 2313283	T3	20090301	ES 2005-702022	20050127
US 20090023725	A1	20090122	US 2006-587790	20060728
PRIORITY APPLN. INFO.:			GB 2004-2143	A 20040130
			WO 2005-GB265	W 20050127

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 143:211906; MARPAT 143:211906

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

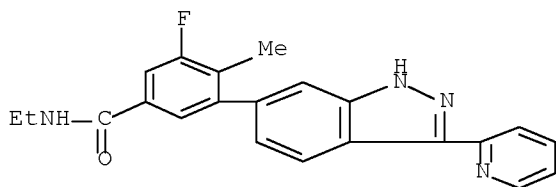
AB Title compds. I [A = (un)substituted fused 5-membered heteroaryl ring, R1 = Me or Cl; R2 = NHCOR3 or CONH(CH2)qR4; R3 = H, alkyl, CF3, etc.; R4 = H, cycloalkyl, alkyl, etc.; q = 0-2; X and Y independently = H, Me or halo] and their pharmaceutically acceptable salts, are prepd. and disclosed as p38 kinase inhibitors. Thus, e.g., II was prepd. by palladium catalyzed Suzuki coupling of 5-bromo-1-phenyl-1H-indazole (prepn. given) with {5-[(cyclopropylamino)carbonyl]-3-fluoro-2-methylphenyl}boronic acid. The activity of I was evaluated in fluorescence anisotropy kinase binding assays and it was revealed that compds. of the invention displayed IC50 values of <10 .mu.M or pKi values of >6. I as p38 kinase inhibitor should prove useful in the treatment of disease states mediated by p38 kinase. Pharmaceutical compns. comprising I are disclosed.

IT 861904-94-1F

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of fused heteroaryl derivs. as p38 kinase inhibitors)

RN 861904-94-1 CAPLUS

CN Benzamide, N-ethyl-3-fluoro-4-methyl-5-[3-(2-pyridinyl)-1H-indazol-6-yl]-
(CA INDEX NAME)



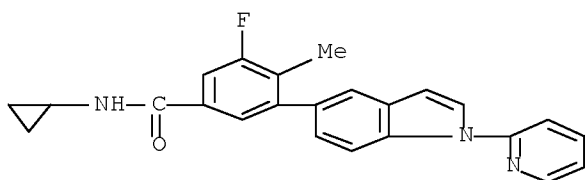
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861905-01-3P 861905-02-4P 861905-03-5P
861905-05-7P 861905-07-9P 861905-08-0P
861905-09-1P 861905-13-7P 861905-15-9P

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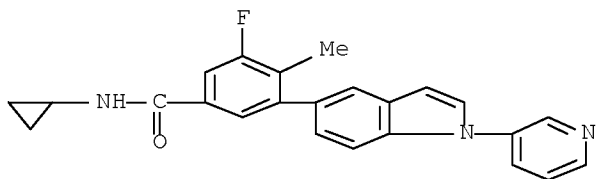
(prepn. of fused heteroaryl derivs. as p38 kinase inhibitors)

RN 861904-46-3 CAPLUS

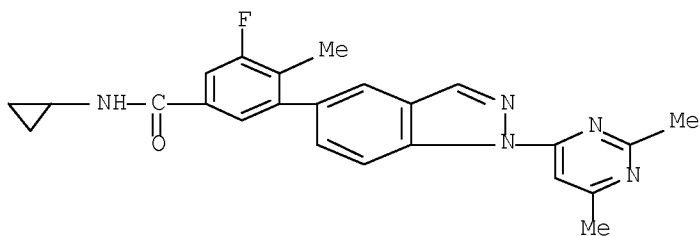
CN Benzamide, N-cyclopropyl-3-fluoro-4-methyl-5-[1-(2-pyridinyl)-1H-indol-5-yl]-
(CA INDEX NAME)



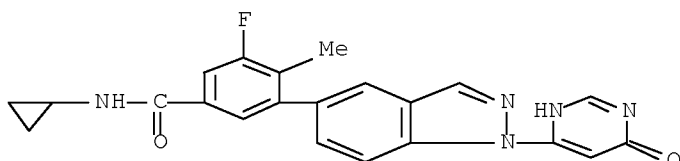
RN 861904-47-4 CAPLUS
 CN Benzamide, N-cyclopropyl-3-fluoro-4-methyl-5-[1-(3-pyridinyl)-1H-indol-5-yl]- (CA INDEX NAME)



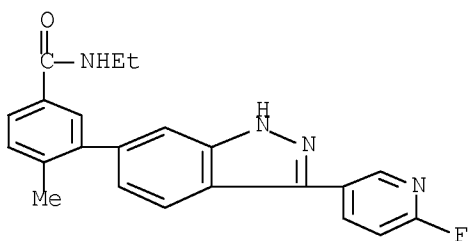
RN 861904-68-9 CAPLUS
 CN Benzamide, N-cyclopropyl-3-[1-(2,6-dimethyl-4-pyrimidinyl)-1H-indazol-5-yl]-5-fluoro-4-methyl- (CA INDEX NAME)



RN 861904-69-0 CAPLUS
 CN Benzamide, N-cyclopropyl-3-[1-(1,6-dihydro-6-oxo-4-pyrimidinyl)-1H-indazol-5-yl]-5-fluoro-4-methyl- (CA INDEX NAME)

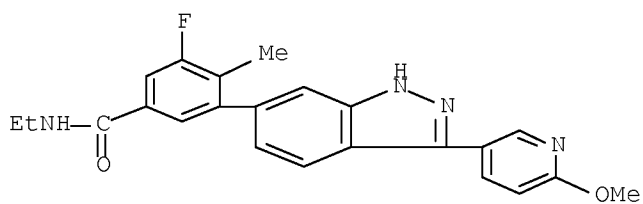


RN 861904-87-2 CAPLUS
 CN Benzamide, N-ethyl-3-[3-(6-fluoro-3-pyridinyl)-1H-indazol-6-yl]-4-methyl- (CA INDEX NAME)



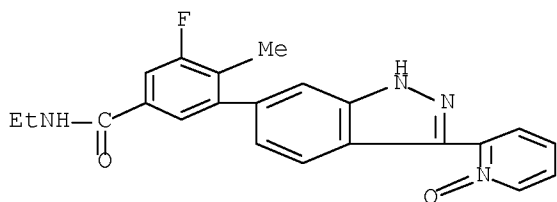
RN 861904-93-0 CAPLUS

CN Benzamide, N-ethyl-3-fluoro-5-[3-(6-methoxy-3-pyridinyl)-1H-indazol-6-yl]-4-methyl- (CA INDEX NAME)



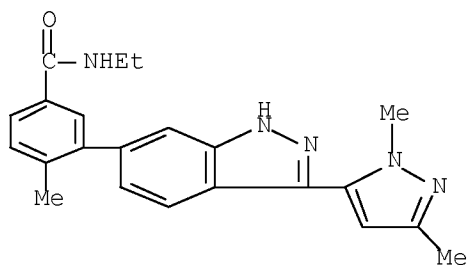
RN 861904-95-2 CAPLUS

CN Benzamide, N-ethyl-3-fluoro-4-methyl-5-[3-(1-oxido-2-pyridinyl)-1H-indazol-6-yl]- (CA INDEX NAME)



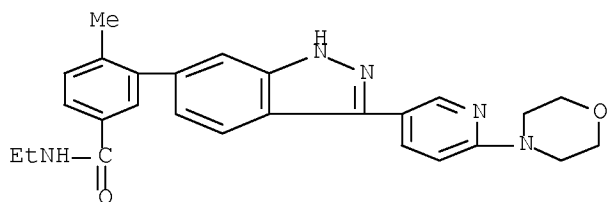
RN 861904-97-4 CAPLUS

CN Benzamide, 3-[3-(1,3-dimethyl-1H-pyrazol-5-yl)-1H-indazol-6-yl]-N-ethyl-4-methyl- (CA INDEX NAME)



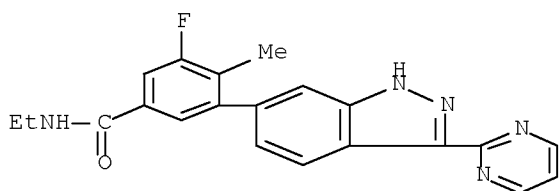
RN 861905-00-2 CAPLUS

CN Benzamide, N-ethyl-4-methyl-3-[3-[6-(4-morpholinyl)-3-pyridinyl]-1H-indazol-6-yl]- (CA INDEX NAME)



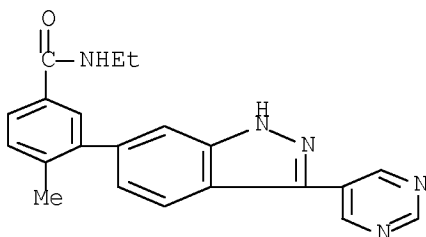
RN 861905-01-3 CAPLUS

CN Benzamide, N-ethyl-3-fluoro-4-methyl-5-[3-(2-pyrimidinyl)-1H-indazol-6-yl]- (CA INDEX NAME)



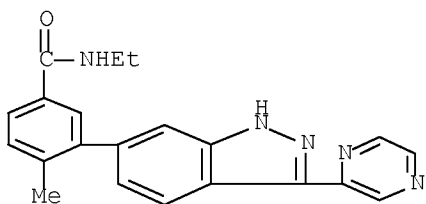
RN 861905-02-4 CAPLUS

CN Benzamide, N-ethyl-4-methyl-3-[3-(5-pyrimidinyl)-1H-indazol-6-yl]- (CA INDEX NAME)



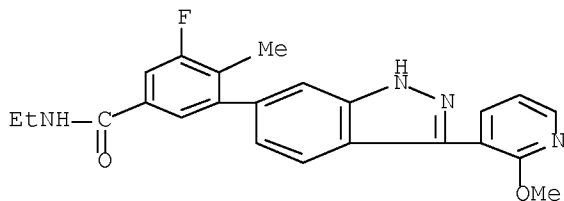
RN 861905-03-5 CAPLUS

CN Benzamide, N-ethyl-4-methyl-3-[3-(2-pyrazinyl)-1H-indazol-6-yl]- (CA INDEX NAME)



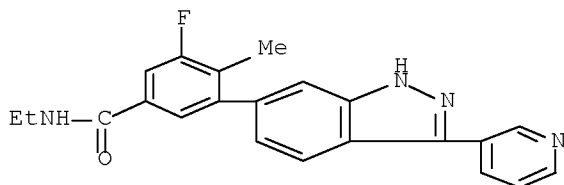
RN 861905-05-7 CAPLUS

CN Benzamide, N-ethyl-3-fluoro-5-[3-(2-methoxy-3-pyridinyl)-1H-indazol-6-yl]-4-methyl- (CA INDEX NAME)



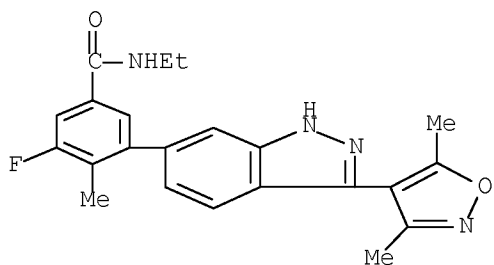
RN 861905-07-9 CAPLUS

CN Benzamide, N-ethyl-3-fluoro-4-methyl-5-[3-(3-pyridinyl)-1H-indazol-6-yl]- (CA INDEX NAME)



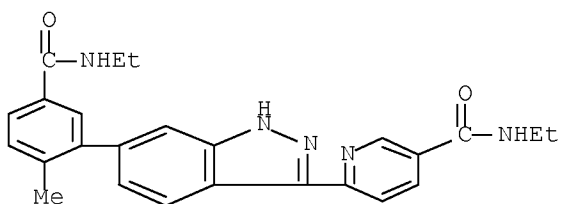
RN 861905-08-0 CAPLUS

CN Benzamide, 3-[3-(3,5-dimethyl-4-isoxazolyl)-1H-indazol-6-yl]-N-ethyl-5-fluoro-4-methyl- (CA INDEX NAME)



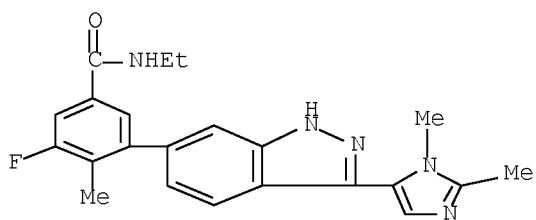
RN 861905-09-1 CAPLUS

CN 3-Pyridinecarboxamide, N-ethyl-6-[6-[5-[(ethylamino)carbonyl]-2-methylphenyl]-1H-indazol-3-yl]- (CA INDEX NAME)



RN 861905-13-7 CAPLUS

CN Benzamide, 3-[3-(1,2-dimethyl-1H-imidazol-5-yl)-1H-indazol-6-yl]-N-ethyl-5-fluoro-4-methyl- (CA INDEX NAME)



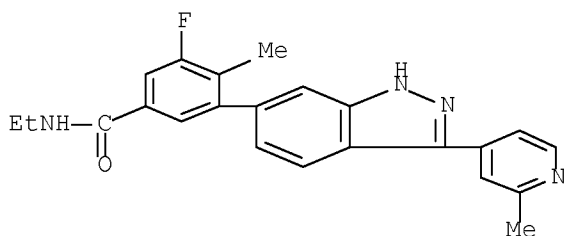
RN 861905-15-9 CAPLUS

CN Formic acid, compd. with N-ethyl-3-fluoro-4-methyl-5-[3-(2-methyl-4-pyridinyl)-1H-indazol-6-yl]benzamide (1:1) (CA INDEX NAME)

CM 1

CRN 861905-14-8

CMF C23 H21 F N4 O



CM 2

CRN 64-18-6

CMF C H2 O2

O=CH-OH

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
 REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:100989 CAPLUS Full-text

DOCUMENT NUMBER: 140:146133

TITLE: Preparation of fused heteroaryls, in particular benzisoxazoles and indazoles, for use as p38 kinase inhibitors in the treatment of rheumatoid arthritis

INVENTOR(S): Angell, Richard Martyn; Baldwin, Ian Robert; Bamborough, Paul; Deboeck, Nigel Marc; Longstaff, Timothy; Swanson, Stephen

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA

SOURCE: PCT Int. Appl., 135 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004010995	A1	20040205	WO 2003-GB3316	20030730
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

AU 2003248978	A1	20040216	AU 2003-248978	20030730
EP 1531812	A1	20050525	EP 2003-771208	20030730
EP 1531812	B1	20070627		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005538100	T	20051215	JP 2004-523985	20030730
AT 365551	T	20070715	AT 2003-771208	20030730
ES 2289336	T3	20080201	ES 2003-771208	20030730
US 20060122221	A1	20060608	US 2005-522955	20051114
US 7642276	B2	20100105		
PRIORITY APPLN. INFO.:			GB 2002-17757	A 20020731
			WO 2003-GB3316	W 20030730
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT				
OTHER SOURCE(S): MARPAT 140:146133				
GI				

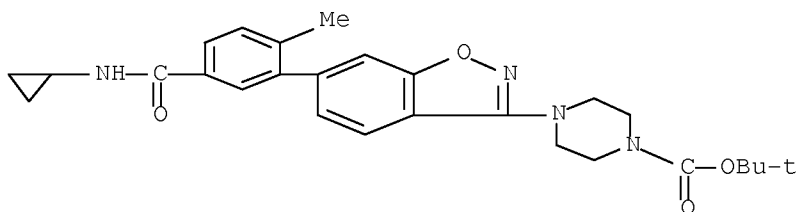
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [wherein ACC = fused 5-membered heteroaryl; R1 = CH3, Cl; R2 = NHCHO and derivs., CONH(CH2)qR3; q = 0-2; R3 = H, cyclo/alkyl, (un)substituted Ph, heteroaryl, etc.; X, Y = independently H, Me, halo] were prepd. as p38 kinase inhibitors for treatment of rheumatoid arthritis. For example, II was prepd. by Pd-cross coupling of 6-bromo-3-piperidin-4-yl-1,2-benzisoxazole and III (prepn. given) at 80.degree. for 18 h. In an in vitro fluorescence anisotropy kinase binding assay, I gave IC50 values < 10 .mu.M for the inhibition of p38 kinase. Thus, I are useful in the treatment of conditions and diseases states mediated by p38 kinase activity or mediated by cytokines produced by the activity of p38, such as rheumatoid arthritis.

IT 651780-05-1P, 1,1-Dimethylethyl
4-[6-[5-[(cyclopropylamino)carbonyl]-2-methylphenyl]-1,2-benzisoxazol-3-yl]-1-piperazinecarboxylate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of fused heteroaryls as p38 kinase inhibitors for treatment of rheumatoid arthritis)

RN 651780-05-1 CAPLUS

CN 1-Piperazinecarboxylic acid, 4-[6-[5-[(cyclopropylamino)carbonyl]-2-methylphenyl]-1,2-benzisoxazol-3-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)

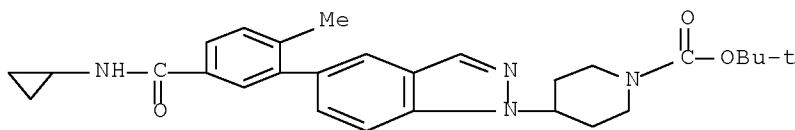


IT 651781-74-7P, 1,1-Dimethylethyl
4-[5-[5-[(cyclopropylamino)carbonyl]-2-methylphenyl]-1H-indazol-1-yl]-1-piperidinecarboxylate
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic

preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(p38 kinase inhibitor; prepn. of fused heteroaryls as p38 kinase inhibitors for treatment of rheumatoid arthritis)

RN 651781-74-7 CAPLUS

CN 1-Piperidinecarboxylic acid, 4-[5-[5-[(cyclopropylamino)carbonyl]-2-methylphenyl]-1H-indazol-1-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



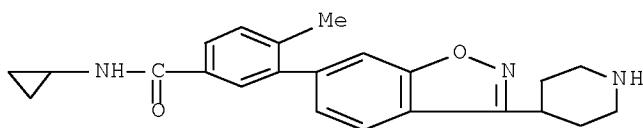
IT 651780-51-7P, N-Cyclopropyl-4-methyl-3-[3-(piperidin-4-yl)-1,2-benzisoxazol-6-yl]benzamide 651780-52-8P,
4-Methyl-N-[3-(morpholin-4-yl)phenyl]-3-[3-(Piperidin-4-yl)-1,2-benzisoxazol-6-yl]benzamide 651780-53-9P,
N-[4-Methyl-3-[3-(piperidin-4-yl)-1,2-benzisoxazol-6-yl]phenyl]-2-(pyrrolidin-1-yl)isonicotinamide 651780-63-1P,
N-(3-Methoxyphenyl)-4-methyl-3-[3-(piperidin-4-yl)-1,2-benzisoxazol-6-yl]benzamide 651780-64-2P,
4-Methyl-3-[3-(piperidin-4-yl)-1,2-benzisoxazol-6-yl]-N-(1,3,4-thiadiazol-2-yl)benzamide 651780-65-3P,
N-[4-Methyl-3-[3-(piperidin-4-yl)-1,2-benzisoxazol-6-yl]phenyl]thiophene-3-carboxamide 651780-66-4P,
N-[4-Methyl-3-[3-(piperidin-4-yl)-1,2-benzisoxazol-6-yl]phenyl]-3-furancarboxamide 651780-67-5P,
N-(Cyclopropylmethyl)-4-methyl-3-[3-(piperidin-4-yl)-1,2-benzisoxazol-6-yl]benzamide 651780-82-4P,
4-Methyl-3-(3-piperidin-4-yl-1,2-benzisoxazol-6-yl)-N-(1,3-thiazol-2-yl)benzamide 651780-83-5P,
N-Cyclopropyl-4-methyl-3-[3-(1-piperazinyl)-1,2-benzisoxazol-6-yl]benzamide 651780-84-6P,
N-Cyclopropyl-4-methyl-3-[3-(morpholin-4-yl)-1,2-benzisoxazol-6-yl]benzamide 651781-75-8P,
N-Cyclopropyl-4-methyl-3-[1-(4-piperidinyl)-1H-indazol-5-yl]benzamide hydrochloride

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(p38 kinase inhibitor; prepn. of fused heteroaryls as p38 kinase inhibitors for treatment of rheumatoid arthritis)

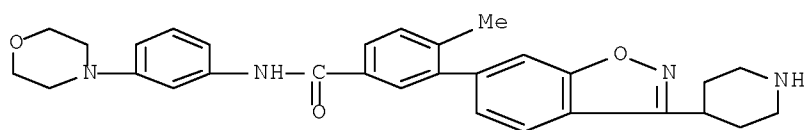
RN 651780-51-7 CAPLUS

CN Benzamide, N-cyclopropyl-4-methyl-3-[3-(4-piperidinyl)-1,2-benzisoxazol-6-yl]- (CA INDEX NAME)



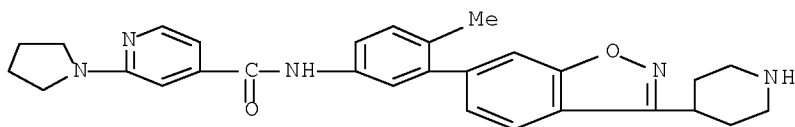
RN 651780-52-8 CAPLUS

CN Benzamide, 4-methyl-N-[3-(4-morpholinyl)phenyl]-3-[3-(4-piperidinyl)-1,2-benzisoxazol-6-yl]- (CA INDEX NAME)



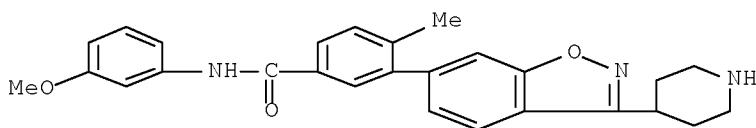
RN 651780-53-9 CAPLUS

CN 4-Pyridinecarboxamide, N-[4-methyl-3-[3-(4-piperidinyl)-1,2-benzisoxazol-6-yl]phenyl]-2-(1-pyrrolidinyl)- (CA INDEX NAME)



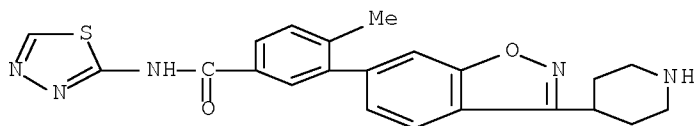
RN 651780-63-1 CAPLUS

CN Benzamide, N-(3-methoxyphenyl)-4-methyl-3-[3-(4-piperidinyl)-1,2-benzisoxazol-6-yl]- (CA INDEX NAME)



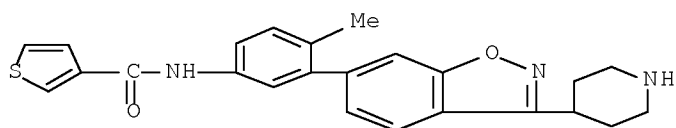
RN 651780-64-2 CAPLUS

CN Benzamide, 4-methyl-3-[3-(4-piperidinyl)-1,2-benzisoxazol-6-yl]-N-1,3,4-thiadiazol-2-yl- (CA INDEX NAME)



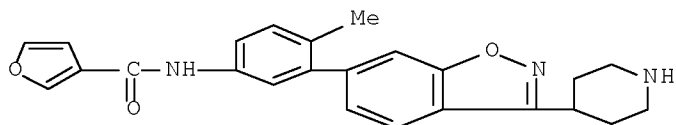
RN 651780-65-3 CAPLUS

CN 3-Thiophenecarboxamide, N-[4-methyl-3-[3-(4-piperidinyl)-1,2-benzisoxazol-6-yl]phenyl]- (CA INDEX NAME)



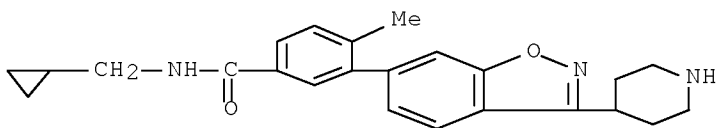
RN 651780-66-4 CAPLUS

CN 3-Furancarboxamide, N-[4-methyl-3-[3-(4-piperidinyl)-1,2-benzisoxazol-6-yl]phenyl]- (CA INDEX NAME)



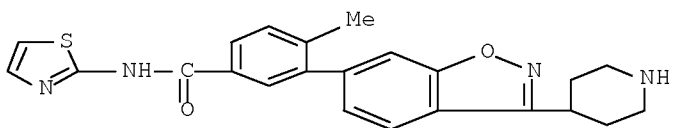
RN 651780-67-5 CAPLUS

CN Benzamide, N-(cyclopropylmethyl)-4-methyl-3-[3-(4-piperidinyl)-1,2-benzisoxazol-6-yl]- (CA INDEX NAME)



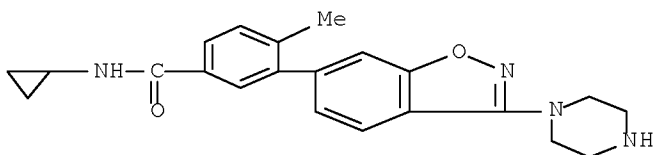
RN 651780-82-4 CAPLUS

CN Benzamide, 4-methyl-3-[3-(4-piperidinyl)-1,2-benzisoxazol-6-yl]-N-2-thiazolyl- (CA INDEX NAME)

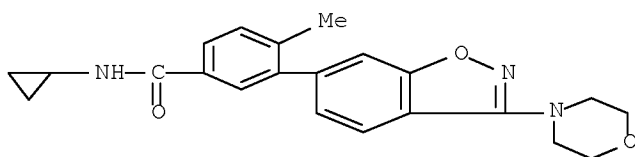


RN 651780-83-5 CAPLUS

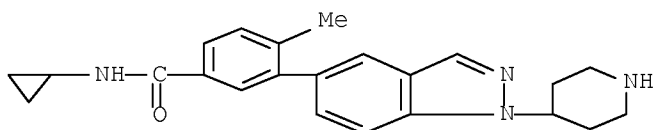
CN Benzamide, N-cyclopropyl-4-methyl-3-[3-(1-piperazinyl)-1,2-benzisoxazol-6-yl]- (CA INDEX NAME)



RN 651780-84-6 CAPLUS
 CN Benzamide, N-cyclopropyl-4-methyl-3-[3-(4-morpholinyl)-1,2-benzisoxazol-6-yl]- (CA INDEX NAME)



RN 651781-75-8 CAPLUS
 CN Benzamide, N-cyclopropyl-4-methyl-3-[1-(4-piperidiny1)-1H-indazol-5-yl]-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

OS.CITING REF COUNT: 18 THERE ARE 18 CAPLUS RECORDS THAT CITE THIS RECORD (18 CITINGS)
 REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2010 ACS on STN
 ACCESSION NUMBER: 2001:851153 CAPLUS Full-text
 DOCUMENT NUMBER: 136:5897
 TITLE: Preparation of benzothiophene derivatives as 17.alpha.-hydroxylase/C17-20 lyase inhibitors
 INVENTOR(S): Shimada, Shinichi; Nomoto, Shin; Okue, Masayuki; Kimura, Kenichi; Nakamura, Junji; Ikeda, Yoshikazu; Takada, Takeko
 PATENT ASSIGNEE(S): Snow Brand Milk Products Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 61 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001087878	A1	20011122	WO 2001-JP4189	20010518
W: AU, CA, CN, HU, IL, JP, KR, MX, NO, NZ, RU, US, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,				

PT, SE, TR

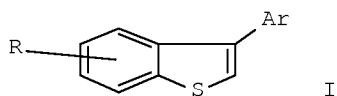
CA 2409821	A1	20021118	CA 2001-2409821	20010518
EP 1283209	A1	20030212	EP 2001-932147	20010518

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR

HU 2003002473	A2	20031128	HU 2003-2473	20010518
NO 2002005475	A	20030115	NO 2002-5475	20021115
US 20030130340	A1	20030710	US 2002-298679	20021118
MX 2002011353	A	20050701	MX 2002-11353	20021118
ZA 2002010202	A	20040317	ZA 2002-10202	20021217

PRIORITY APPLN. INFO.: JP 2000-146579 A 20000518
WO 2001-JP4189 W 20010518

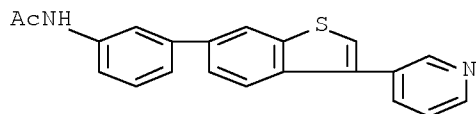
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 136:5897
GI



AB The title compds. I [Ar is a substituted or unsubstituted arom. heterocyclic group; and R is amino which may be mono- or di-substituted with one or more members selected from among hydroxyl, lower alkyl, lower alkyloxy, halogeno, carboxyl, lower alkyloxycarbonyl, carbamoyl, amino, lower alkyl, and lower acyl ; cyano; optionally substituted phenyl; optionally substituted phenoxy; optionally substituted phenyl-lower alkyl; optionally substituted phenyl-lower alkyloxy; or an optionally substituted arom. heterocyclic group] are prepd. 3-(6-Isopropoxybenzo[b]thiophen-3-yl)pyridine hydrochloride at 300 nM gave 100% inhibition of 17.alpha.-hydroxylase/C17-20 lyase.

IT 374753-66-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of benzothiophene derivs. as 17.alpha.-hydroxylase/C17-20 lyase inhibitors)

RN 374753-66-9 CAPLUS
CN Acetamide, N-[3-[3-(3-pyridinyl)benzo[b]thien-6-yl]phenyl]- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2001:12273 CAPLUS Full-text

DOCUMENT NUMBER: 134:86271

TITLE: Preparation of pyrimidine derivatives as Src-family protein tyrosine kinase inhibitor compounds

INVENTOR(S): Armstrong, Helen M.; Beresis, Richard; Goulet, Joung L.; Holmes, Mark A.; Hong, Xingfang; Mills, Sander G.; Parsons, William H.; Sinclair, Peter J.; Steiner, Mark G.; Wong, Frederick; Zaller, Dennis M.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 470 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

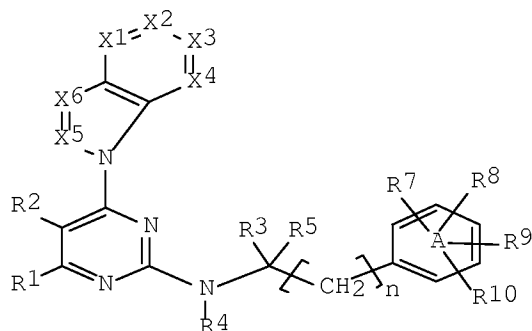
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000213	A1	20010104	WO 2000-US17443	20000626
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2383546	A1	20010104	CA 2000-2383546	20000626
EP 1206265	A1	20020522	EP 2000-941701	20000626
EP 1206265	B1	20031112		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			
US 6498165	B1	20021224	US 2000-604305	20000626
JP 2003523942	T	20030812	JP 2001-505922	20000626
AT 253915	T	20031115	AT 2000-941701	20000626
PRIORITY APPLN. INFO.:			US 1999-141639P	P 19990630
			WO 2000-US17443	W 20000626

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): MARPAT 134:86271

GI



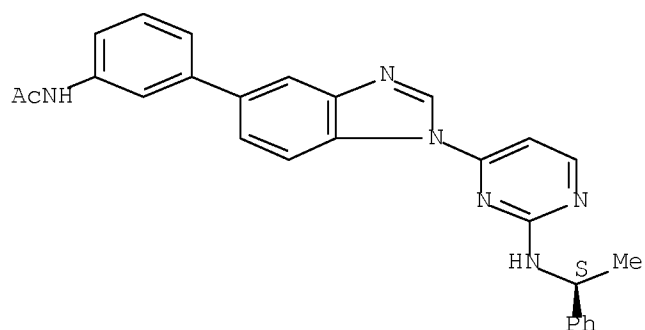
AB What are claimed are pyrimidine compds. (shown as I), or their pharmaceutically acceptable salts, hydrates, solvates, crystal forms and individual diastereomers, and pharmaceutical compns. including the same and their use as inhibitors of tyrosine kinase enzymes and consequently their use in the prophylaxis and treatment of protein tyrosine kinase-assocd. disorders, such as immune diseases, hyperproliferative disorders and other diseases in which inappropriate protein kinase action is believed to play a role, such as cancer, angiogenesis, atherosclerosis, graft rejection, rheumatoid arthritis and psoriasis. In I, R1, R2 = independently H, halo, OH, SH, CN, NO2, alkyl, alkoxy, acyloxy, alkoxycarbonyloxy, carbamoyloxy, alkylthio, sulfinyl, sulfonyl, acyl, alkoxycarbonyl, carbamoyl, amino, acylamino, ureido, sulfamoyl, sulfonylamino, or R1 and R2 can join together to form a fused methylenedioxy ring or a fused 6-membered arom. ring; terms such as 'alkyl' here and below are further defined in the claims. R3, R5 = independently H, C1-C6-alkyl unsubstituted or substituted with 1-3 substituents, aryl, or R3 and R5 taken together can represent :O; R3 or R5 can represent a 2 or 3 C methylene bridge forming a ring of 5-8 atoms fused to the A ring. R4 = H, C1-C6-alkyl, C1-C6-alkoxyl. X1, X2, X3, X4 in -X1:X2-X3:X4- are substituted or unsubstituted CH or N where 0-2 of X1, X2, X3, X4 are N. X5, X6 = independently N, C, optionally substituted CH. A ring = Ph, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyrrolyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, pyrazolyl, triazolyl, tetrazolyl, furanyl, benzothienyl, benzofuranyl, indolyl, imidazolyl, benzimidazolyl, thiadiazolyl. R7, R8, R9, R10 = independently H, halo, OH, SH, CN, NO2, N3, N2+BF4-, alkyl, alkoxy, alkylthio, sulfinyl, sulfonyl, C1-C6-alkyl, C1-C6-perfluoroalkyl, acyl, alkoxycarbonyl, carbamoyl, acyloxy, alkoxycarbonyloxy, carbamoyloxy, amino, acylamino, ureido, sulfamoyl, sulfonylamino, two of R7, R8, R9, and R10 when on adjacent carbons join together to form a methylenedioxy bridge. N = 0-2. More than 500 example prepn. are given, but no preparative method is claimed and no data relating to the usefulness of the compds. are given. [This abstr. record is one of 2 records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.]

IT 317827-90-0P, 2-[(S)-1-Phenylethylamino]-4-[5-(3-N-acetylaminophenyl)benzimidazol-1-yl]pyrimidine
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of pyrimidine derivs. as Src-family protein tyrosine kinase inhibitor compds.)

RN 317827-90-0 CAPLUS

CN Acetamide, N-[3-[1-[2-[(1S)-1-phenylethyl]amino]-4-pyrimidinyl]-1H-benzimidazol-5-yl]phenyl]- (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS
 RECORD (17 CITINGS)
 REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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Executing the logoff script...

=> LOG H

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	53.29	302.81
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-7.65	-7.65

SESSION WILL BE HELD FOR 120 MINUTES
 STN INTERNATIONAL SESSION SUSPENDED AT 18:46:17 ON 01 FEB 2010